DETAILED ACTION

Status of the claims

Claims 1-36 are pending.

The amendment filed 1/24/06 which amends claims 10-11, 13, and 22 has been entered. The applicants' request filed 7/16/08 for extension of time of two months has been entered.

Foreign priority

Applicants' claim for foreign priority under 35 U.S.C. 119 (a)-(d) is acknowledged. The copy of the United Kingdom 0317944.7 and filed 7/31/03 and 0317945.4 filed 7/31/03 has been received.

Election/Restrictions

Applicant's election (filed 7/16/08) of Group I, claims 1-25 and further election of yeast RAD54 gene for examination without traverse is acknowledged. Claims 11-12 are drawn into yeast RNR regulatory element other than the elected "RAD54", and thus, claims 11-12 are withdrawn from further consideration. Since the vectors of claim 18 (Fig. 24, "pGenRNR2") and claim19 (Fig. 25, "GenRNR3") are constructed from non-elected "RNR2" and "RNR3", respectively, claims 18 and 19 are withdrawn from further consideration as well. Claims 26-36 are drawn into non-elected invention; and thus, are withdrawn from further consideration by the examiner, 37 CFR 1.142(b). Claims 1-10, 13-17, and 20-25 are examined in this Office action.

Objection to Specification

(1) At page 2, 4th paragraph, line 3, "yEGFP" should be spelled out for the first instance of use. See also page 12, 2nd paragraph, line 6, "HO"; and, page 22, the description of Figure 1, line 4, "MMS".

(2) At page 10, 3rd paragraph, line 6, the meaning of "between co-ordinates 387100-393299" should be clarified.

(3) At page 13, last paragraph, line 3, "Fig:42" should be changed to "Figure 37" for consistence reason.

(4) At page 14, 1st paragraph, line 3, After "*HO* (HO int)" should insert "gene" for clarity.

(5) At Page 25, the description of Figure 15, line, "presentinvention" should be changed to "present invention".

(6) The brief description of Figure 34 at page 26 is objected to because it does not provide description of panels (a) and (b) as depicted in the figure.

(7) At page 46, 3rd paragraph, line 2, "pWDH4454" should be changed to "pWDH445".

Objection to drawings

(1) drawings are objected becasue "Fig:30", "Fig:31", "Fig:32", "Fig:33", "Fig:34", "Fig:35", "Fig:36", "Fig:37", "Fig:38", "Fig:39", "Fig:40", "Fig:41", and "Fig:42" should be changed to ""Fig.30", "Fig.31", "Fig.", "Fig.3", "Fig.4", "Fig.5", "Fig.6", "Fig.7", "Fig.8", "Fig.9", "Fig.0", "Fig.1", and "Fig.2", respectively, for consistence.

(2) Fig. 5 which shows the restriction map of pWDH445" should be designated by a legend such as "Prior Art" because, at page 9, 5th paragraph, the instant specification has taught that "pWDH445" is equal to "yEGP-44" of prior art WO9844149. See MPEP § 608.02(g). A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Objection to claims

• Claim 8 is objected to because after "DNA encoding", the term "for" should be deleted; and, because "HO" should be spelled out in full for the first time recitation in the claims; similarly, see claim 11, "RNR".

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 1-10, 13-17, and 20-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 should make it clear in which order (i) the DNA encoding reporter protein (claim 1), (ii) regulatory element" (claim 1), (iii) DNA of "2μ plasmid" (claim 6), (iv) DNA of part of "HO" gene (claim 8), (v) nucleotide sequence of the ribosomal DNA array (claim 9), and (vi) nucleotide sequence of "kanMX" module (claim 14-16) are organized into the disclosed vector. This is because, in general, orientation between regulatory element and gene(s) is important for transcription (see "*Discussion of art*" [1]), and also see instant Figures 5 and 38). Claims 2-10 and 13-25 which depend from claim 1 are also rejected.

Claim 6 does not make it clear what portion of the DNA of "2μ plasmid" is contained in the vector; does it refer to entire "2μ plasmid" or/and part of, e.g., origin of replication section, said plasmid?

Claim 9 is indefinite in "any one of claims 7" (incomplete recitation).

Claim 10 is not apparent as to whether or not "the regulatory element" comprises an entire "yeast RAD54 gene", or the promoter region (non-coding region) or/and coding region of RAD54 protein.

Claims 17-21 should make it clear what the "functional derivative" of the claimed "vector" refer. The specification does not define the "functional derivative" thereof; what does it differ from the structural derivative of the vector? *Examiner comments*:

The recitation of claim 1"does not substantially alter the sensitivity of the cell to geneticin" has been taught in the specification (page 4, 3rd paragraph), i.e., "it means that the sensitivity to geneticin of a cell which has been transformed with the vector according to the first aspect of the invention is at least 70% that of the sensitivity to geneticin of a cell which has not been transformed with the vector". Thus, said recitation is not indefinite.

Examiner comments:

(i) The specification has describe and provided enablement for "part of the HO gene" in claim 8 because the specification teaches that fragments of the HO gene from chromosome IV of S. cerevisiae favours targeted integration in S. cerevisiae or cell lines derived therefrom. (see Figure 35 and page 12, 2nd paragraph).

(ii) The specification has described and provided enablement for "non-functional kanMX module" in claims 14-16, because in Example 1, pages 44-50, the specification has taught the "kanMX module" is used as a convenient selectable marker and loss of said module remove interference of efficient transcription of reporter protein (GFP) gene.

(iii) The specification enables "derivative of Green Fluorescence Protein (GFP)" (claims 2-4), because, when the invention was made, the bioactive GFP mutants/derivatives have been known in the relative art and thus by one skilled in the art.

Claim Rejections - 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

[1] Claims 1-2, 5, 7, 10, 17, 20-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Essers et al. (*EMBO J.* (2002) 21, 2030-2037).

Essers et al teach a DNA construct (plasmid) "RAD54-GFP" comprising GFP which is a reporter protein and RAD54, which anticipates claims 1-2 and 10.

The plasmid has inherent property of autonomously replicate in the cell in which the plasmid is transformed; and thus, Essers et al. anticipate claim 5.

Because this "RAD54-GFP" is fully functionally in DNA repair and recombination (a mechanism of DNA integration into host genome) (see page 2031, left column, lines 20-22), Essers et al. teach claim 7.

The Essers' plasmid is considered to be a functional derivative of vector of claim 17, 20, or 21, respectively; and thus, claims 17 and 20-21 are included in the rejection.

Figure 2A of Essers et al. shows a single cell line comprising said "DNA construct" (see also page 2031, left column, 2nd paragraph, lines 16-17), which anticipates claim 22.

[2] Claims 1-10, 13-17, and 20-25 are under 35 U.S.C. 102 (b) as being anticipated by Billinton et al. (*Biosen. Bioelect.* (1998) 13, 831-838).

Billiton et al. teach a recombinant vector "pWDH443" (see page 832, Figure 1) comprising RAD54 promoter (regulatory element) operationally linked to down stream "GFP" (reporter protein) gene where in "GFP" is "S65T" variant (Table 2), 2μ DNA segment, kanMX3 sequence, a fragment of HO gene, which anticipates claims 1-3, 6, 8, 10, 14-16,

The GFP is "yEGFP", i.e., "yeast enhanced GFP" (see page 833, right column, line 3), which anticipates claim 4.

The vector has inherent property of autonomously replicate in the yeast cell in which the vector is transformed; and thus, Billiton et al. anticipate claim 5.

The vector having property of multiple copies capable of target to chromosome of host via sequence from the ribosomal DNA array (page 837, right column, lines 7-10), i.e., capable of integrate into the chromosome, which teaches claim 7 and 9.

Since "pWDH443" inherently contains 'pFA" DNA sequence (see "*Discussion of art*" [3]), Billiton et al. teach claim 13.

The "pWDH443" is considered to be functional derivative of the vectors recited in claims 17, 20 and 21, and thus, Billiton et al. teach claims, 17, 20 and 21.

Billiton et al. teach a *S. cerevisiae* strain "F18984" (Table 1, page 832), which anticipates claims 22-25.

[3] Claims 1-10, 13-17, and 20-25 are under 35 U.S.C. 102 (b) as being anticipated by Walmsley et al. (WO 98/44149); for confidence US Pat. equivalent (US 6489099) is cited here.

At patent claims 12, 14-15, and Figures 11-12, Walmsley et al. teach recombinant vectors "pWDH443" and "pWHD444" comprising RAD54 promoter (regulatory element) operationally linked to down stream "GFP" (reporter protein) gene where in "GFP" is "S65T" variant (patent claim 3), 2μ DNA segment, kanMX3 sequence, a fragment of HO gene, which anticipates instant claims 1-3, 6, 8, 10, 14-16,

The GFP is "YEGFP" which stands for "yeast enhanced GFP" (see patent claim 13 and col. 3, lines 47-48), which anticipates instant claim 4.

The vector has property of autonomously replicate in the transformed host cell (patent claim 6), which anticipates instant claim 5.

The vector having property of integrating into host genomic DNA (patent claim 8) via sequence from the ribosomal DNA array (col. 4, lines 46-47), which anticipates claims 7 and 9.

The vector is derived from 'pFA" plasmid (patent claim 10), which anticipates instant claim 13.

The "pWDH443" or 'pWHD444" is considered to be functional derivative of the vectors recited in claims 17, 20 and 21, and thus, Walmsley et al. teach claims, 17, 20 and 21.

Walmsley et al. teach a *S. cerevisiae* strain "F18984" in haploid form (patent claim 22), which anticipates instant claim 22-25.

Conclusion

No claims are allowed.

Discussion of the art

The prior art made of record and not currently relied upon in any rejections is considered pertinent to Applicants' disclosure:

[1] Weaver et al. (*Proc. Natl. Acad. Sci. USA*. (2007) 44, 2813-2819) teach that orientation between regulatory and core promoter of a gene is important for setting the level of transcription (see abstract) because the reverse orientation resulted in lower level of induced expression (page 7, 2nd paragraph, lines 9-11).

[2] Walsh et al. (*Mutagenesis* (2005) 20, 317-327) teach a recombinant vector comprising GFP optionally linked to the regulatory element, i.e., upstream non-coding sequences of the RAD54 gene, and yeast strain "FF18984" transformed with said vector (see "Material and methods" section), which teach instant claims 1-2, 5, 7, 10, 17 and 20-25. Yet, this reference is not the prior art because it does not antedate the instant invention.

[3] Walmsley et al. (US Pat. No. 7049071 B2) teach that "pWDH443" contains 'pFA" DNA sequence (see col. 5, line 10).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is 571-272-0949. The examiner can normally be reached from 9:00 a.m. to 5:00 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragton, can be reached on (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

/Samuel W Liu, Ph.D./

Examiner, Art Unit 1656

October 8, 2008

/Karen Cochrane Carlson, Ph.D./
Primary Examiner, Art Unit 1656